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# INTERNATIONAL PRELIMINARY EXAMINATION REPORT



(PCT Article 36 and Rule 70)

Applicant's or agent's file reference Case 21307	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP 03/04893	International filing date (day/month/year) 09.05.2003	Priority date (day/month/year) 04.07.2002
International Patent Classification (IPC) or both national classification and IPC C12P7/26		
Applicant DSM IP ASSETS B.V. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
  - ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of    sheets.

3. This report contains indications relating to the following items:
  - I ☒ Basis of the opinion
  - II ☐ Priority
  - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - IV ☐ Lack of unity of invention
  - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - VI ☐ Certain documents cited
  - VII ☐ Certain defects in the international application
  - VIII ☐ Certain observations on the international application

Date of submission of the demand  23.12.2003	Date of completion of this report  18.08.2004
Name and mailing address of the international preliminary examining authority:   European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer  Smalt, R  Telephone No. +31 70 340-4275  

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/EP 03/04893**

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-7 as originally filed

**Sequence listings part of the description, Pages**

1 as originally filed

**Claims, Numbers**

1-13 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.  
☒ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	5,11
	No: Claims	1-4,6-10,12,13
Inventive step (IS)	Yes: Claims	
	No: Claims	1-13
Industrial applicability (IA)	Yes: Claims	1-13
	No: Claims	

2. Citations and explanations

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP 03/04893

1. The following **documents** (D) are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

- D1: WADA M ET AL: 'PURIFICATION AND CHARACTERIZATION OF MONOVALENT CATION-ACTIVATED LEVODIONE REDUCTASE FROM CORYNEBACTERIUM AQUATICUM M-13' APPLIED AND ENVIRONMENTAL MICROBIOLOGY, WASHINGTON,DC, US, vol. 65, no. 10, October 1999 (1999-10), pages 4399-4403, XP000910999 ISSN: 0099-2240
- D2: EP-A-1 122 315 (HOFFMANN LA ROCHE) 8 August 2001 (2001-08-08)
- D3: EP-A-0 982 406 (HOFFMANN LA ROCHE) 1 March 2000 (2000-03-01)

**1. Novelty (Art.33(2) PCT)**

D1 describes the purification of the levodione reductase from *Corynebacterium aquaticum M-13*, as used in the present application. The enzyme is primarily used for the regio- and stereospecific conversion of levodione into actinol, but table 3 shows that ketoisophorone can also serve as a substrate for this enzyme. The latter differs from levodione in that it has a double rather than a single bond between carbon atoms 5 and 6, and the corresponding enzymatic reduction of the keto group on the 4 position would yield phorenol. The applicants argumentation that the third paragraph in the right-hand column on page 4401 of D1 shows that ketoisophorone is in fact converted to actinol rather than phorenol could not be followed; what is shown is that the enzymatic conversion levodione + NADH + H<sup>+</sup>  $\rightleftharpoons$  actinol + NAD<sup>+</sup> is reversible. The notion that regardless of which substrate is chosen from table 3, the enzyme always produces actinol, cannot be chaired with the applicant. From table 1 it is suggested that functionally similar enzymes can be obtained from *Arthrobacter sulfureus* AKU635, *Flavobacterium/ Planococcus okeanokoites* AKU152 and *Cellulomonas cellulans* AKU672. In the light of D1, the present claims 1-4,6-10,12 and 13 are not new.

**2. Inventive step (Art.33(3) PCT)**

Strictly speaking, the isolation or use of levodione reductase enzyme specifically from the *Corynebacterium aquaticum M-13* AKU611 strain is not explicitly disclosed in D1. However, the isolation of this enzyme from *Corynebacterium aquaticum M-13* AKU611 is described in D2, which furthermore suggests cloning of similar enzymes from *Cellulomonas*, *Planococcus* and *Arthrobacter*. In D3 the cloning of these enzymes from the isolates as indicated above, and also from *C. aquaticum* AKU610, is described (see

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e.g. passage 7-8 and tables III-V). Claims 5 and 11 can therefore not be considered to contribute an aspect, which alone or in combination with the subject-matter of the other claims can be considered as involving an inventive step.